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FROZEN RED BLOOD CELLS IN COMBAT CASUALTY CARE: CLINICAL AND LOGISTIC CONSIDERATIONS

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ABSTRACT

OBJECTIVE: To test the hypothesis that a supply of frozen red blood cells and a system for processing sterile pyrogen-free crystalloid solution would meet the needs of an Echelon 3 medical treatment facility caring for combat casualties during the initial phase of a military medical operation.

DATA SOURCES: Blood requirements for potential combat casualties were estimated from transfusion data on: 1) patients admitted to Boston City Hospital following trauma, utilizing a computerized database; 2) patients admitted to the Naval Support Hospital - Da Nang during the Vietnam War, from 1966 to 1970, from published and unpublished material; 3) casualties estimated by Department of Defense expert panels for specific conflicts. The procedure for processing frozen red blood cells was evaluated at the Naval Blood Research Laboratory in Boston. Estimates of wounded-in-action were provided by the Department of Defense.

DATA SYNTHESIS: Computer modeling using standard spreadsheet software on a personal computer.

conclusions: Under military conditions, a frozen blood bank and a system for processing sterile pyrogen-free resuscitative fluid could be used to prepare 110 units of red cells and 960- liters of crystalloid per day. This

would be adequate to treat approximately 170 casualties, the number projected for a 5-day battle with heavy casualties (6 wounded-in action/1000 soldiers/day). It was concluded that a frozen blood bank system and a system for processing sterile pyrogen-free resuscitative fluid could successfully meet the needs of an Echelon 3 medical facility in the initial phase of a military medical operation.

INTRODUCTION

During the recently completed Operation Desert Storm, approximately 81,000 units of liquid preserved red blood cells were delivered to the Middle East for potential casualty care. In future conflicts, military medical facilities may be expected initially to rely on frozen blood banks to supply red cells, platelets and plasma until liquid blood is available.1

Frozen red blood cells were first used to treat combat casualties during the Vietnam conflict. Moss et al2,3 and Valeri4 demonstrated that frozen red blood cells were both safe and therapeutically effective in the combat setting. The FDA has approved the method described by Valeri and associates5 to freeze red blood cells for 10 years of forzen storage at -80 C and 24 hours of post-thaw-wash storage at 4 C. The Department of Defense will permit 3 days of post-wash storage at 4 C in emergency situations.

The plan is to pre-position large supplies of frozen red blood cells on land and aboard ships readily available in emergency situations. However, before a combat casualty care program that relies primarily on frozen red cells can be implemented, certain clinical and logistic issues must be resolved.

Large volumes of pyrogen-free crystalloid solution are also necessary for the care of mass casualties. The goal now is to be able to manufacture sterile pyrogen-free lactate solutions at military medical facilities in the field or at sea. This system, currently being evaluated, utilizes filters and membranes in the production of crystalloid solutions used for resuscitation and solutions necessary for the deglycerolization of frozen red blood cells.

A review of the organization of health care in the combat theater is useful in understanding the logistical issues involved. Medical care is organized in a multitiered system of four levels of increasing capabilities. Echelon 1 medical facilities are limited to preparation of the seriously injured for evacuation, including maintenance of the airway, control of hemorrhage and initiation of intravenous fluid administration; no blood is available at this level. This is the equivalent of a first-aid station or paramedic unit in the civilian setting. Echelon 2 medical facilities are capable of more advanced interventions, including resuscitation and initial surgery. Echelon 3 facilities are staffed and equipped for surgery and post-operative care equivalent to a Level I trauma center. Echelon 4 facilities have the capacity of all of the previous echelons of care and, in addition, are equipped for follow-up surgery and rehabilitation. Current military

plans include pre-positioning of frozen blood banks at Echelon 3 and Echelon 4 facilities.6

The study reported here was undertaken to test the hypothesis that a supply of frozen red blood cells and a system for processing a sterile pyrogen-free crystalloid solution could meet the needs of an Echelon 3 facility caring for casualties during the initial phase of military medical operation. To test this hypothesis, we obtained data from various medical sources in an attempt to estimate crystalloid requirements. The logistic capacity of a frozen blood bank can be identified by integrating the estimates of red blood cell and crystalloid requirements. This approach is similar to that recently advocated by Bowersox who used a database incorporating civilian trauma experiences to estimate supply requirements during combat casualty care.7

MATERIALS AND METHODS

BLOOD AND CRYSTALLOID REQUIREMENTS

In this study, blood requirements were estimated from a variety of sources, such as civilian and military clinical experiences and the review of current military planning documents.

Transfusion requirements for specific injuries may vary widely from patient to patient but are relatively predictable depending on the severity of injury. An acceptable method for estimating the degree of blood loss associated with an injury is the "Class of Acute Hemorrhage System" as described in the Advanced Trauma Life Support (ATLS) Handbook of the American College of Surgeons.8 This system, which is driven by clinical findings, categorizes blood loss into four classes (Table 1).

In reviewing the trauma experiences at the Boston City Hospital, a civilian Level 1 trauma center, we used the trauma registry to identify significantly injured patients who by clinical and laboratory parameters (pH < 7.25) were estimated to be in Class IV hemorrhage.9

Data collected at the Naval Support Activity Hospital-Da Nang (an Echelon 3 facility) during the Vietnam conflict were reviewed to estimate total blood usage for a large number of moderately to severely wounded-in-action (WIA). These data were obtained from records of blood utilization over a three-year period, and included numbers of units transfused, numbers of procedures performed, and the number of units transfused per casualty.10

The Department of Defense Deployable Medical Systems (DEPMEDS) manual, the military document which outlines the logistics of medical services in the theater of combat, contains an extensive compendium of possible combat casualty scenarios. Review of patient conditions in this document, which are classified by ATLS classes of hemorrhage and the estimated need for blood transfusions, provided the third independent estimation of blood utilization based on injury classification by degree of hemorrhage.11

Medical casualty tables for multiple casualty scenarios developed by the Department of Defense based on historical information were used to estimate the relative distribution of injury severity in combat situations.12

Department of Defense estimates of casualty rates per 1000 combatants per day were used to calculate a patient load for an Echelon 3 medical treatment facility.13

Using the above estimates of blood and fluid requirements, a computer model was created using spreadsheet software (Excel, Microsoft, Redmond, WA) on a personal computer to calculate red blood cell and crystalloid requirements for casualties incurred during a battle. The simulation took into account the duration of hostilities, the number of casualties, the magnitude of injury, and the site of initial resuscitation and subsequent treatment. This model is unique in that it projected both daily and cumulative utilization of blood and crystalloid at a medical treatment facility. Projection of daily usage is central to testing the hypothesis that an Echelon 3 facility can meet its entire needs using frozen red blood cells and crystalloid processing systems, especially at the time of maximum demand.

FROZEN RED CELL PROCESSING

Red blood cells frozen with glycerol must be washed after thawing to reduce the residual glycerol concentration to less than 1%. The Haemonetics Blood Processor 115 (Haemonetics, Braintree, MA) is used to wash the glycerolized red blood cells using a solution containing 50 ml of 12% sodium chloride and 1.5 liters of 0.9% sodium chloride and 0.2 gm% glucose.5 Disposable tubing and bags and wash solutions are also necessary for the deglycerolization process. Trained personnel must be

available to perform the necessary steps in the deglycerolization process.

Productivity exercises to test the efficiency of personnel involved in the processing of frozen red blood cells have have been undertaken at the Naval Blood Research Laboratory (Boston, MA). Following one day of training, a single technician was able to operate three Haemonetics Blood Processor 115 machines at a time, with each machine preparing 1 unit of frozen red blood cells per hour. In a sustained effort of 12 hours, each technician was capable of preparing 36 units of deglycerolized red blood cells while running three processors. Under extreme conditions, a single technician should be able to operate 4 Haemonetics Blood Processor 115 machines; however the productivity of the individual cell washers has been shown to diminish to 0.95 units/hour. This amounts to 3.8 units RBC/hour/technician, which results in 45.6 units of deglycerolized red blood cells over a 12-hour period.14 The number of available red blood cell units processed will depend upon the number of processors and technicians positioned at an Echelon 3 facility. Currently these facilities are supported by four processors and personnel to process frozen blood 22-24 hours/day.

Plans are in place for the preparation of a 0.9% sodium chloride-0.2 gm% glucose deglycerolization solution at the

site of need. Tests are being conducted on the

Resuscitative Fluid Production System (REFLUPS) which

utilizes membranes and filters to produce sterile pyrogen
free solutions at the rate of 40 liters per hour.

UTILIZATION OF RED BLOOD CELLS IN THE OPERATING ROOM

The volume of red blood cells used in the operating rooms will depend upon the number of casualties and the severity of the injuries, as well as the availability of operating rooms and personnel to care for such patients. Estimates of the numbers of red blood cell units required were based on several assumptions: that all the patients in Class 3 and IV hemorrhage and 50% of Class 2 patients would require major operations, and that 70% of the casualties would have extremity injuries that would require a second operation by hospital day 3.

RESULTS

The Boston City Hospital Trauma Registry identified 107 patients who presented with evidence of a significant blood loss, as indicated by an arterial blood gas of pH <7.25 on admission. This represents a physiological derangement that is indicative of major blood loss, consistent with a Class IV hemorrhage. These patients required an average of 13.6 units of transfused blood during their total hospital stay.

Review of data on blood usage at the Naval Support Activity Hospital, Da Nang, Republic of Vietnam, from 1966 to 1970 revealed that the overwhelming majority of injured (>80%) required minimal blood transfusion (0 to 1 unit of RBC) for their resuscitation. Only a small number of patients (<5%) required 6 or more units of blood; most of the patients who did require blood transfusions received an average of 3 units of red blood cells. Information correlating severity of injury and blood requirements is limited to data regarding the surgical environment in which care was rendered (i.e. operating room vs minor operating suite vs no operative procedure required).

A review of the 325 patient conditions (PCs) listed in the DEPMEDS Patient Database demonstrated that 27 PCs classified as Class IV hemorrhage averaged 15.85 units of blood transfused. Thirty three (33) PCs classified as Class 3 hemorrhage averaged

3.85 units of blood transfused. Thirty-one (31) PCs classified as Class 2 hemorrhage averaged 2.25 units of blood transfused.

The scenarios of large-scale battles and the casualty estimates for three different geographic conflicts provided estimates of casualties triaged to an Echelon 3 level facility. These estimates, based on past military experience, demonstrate that although the majority of wounded in action are expected to suffer some degree of hemorrhage (73-76%), about 32% of these would be suffering Class II shock (32%). Although only 12-13% of WIA are expected to be in Class IV shock, these would be the casualties who would require the greatest number of blood transfusions (50-54%).

It has been estimated that there would be 3 or less wounded-in-action (WIA) per 1000 soldiers per day in a low-intensity conflict, and that this would increase to 6 WIA per 1000 soldiers per day in a high-intensity conflict. An Echelon 3 facility could support an estimated 6000 troops, front-line and support personnel combined, representing up to 36 casualties per day.

Using the estimates of blood and fluid requirements determined from these various sources (Table 2), a computer simulation was done of the treatment of 6 WIA/1000 soldiers/day at an Echelon 3 facility during a five-day conflict.

The simulation algorithm can adjust for wounded who receive treatment in Echelon 1 and 2 facilities prior to their transfer to an Echelon 3 facility. Frozen red cells are not currently available for transfusion at either Echelon 1 or 2 facilities. Casualties treated initially at these facilities would be resuscitated under standard treatment protocols prior to transfer to an Echelon 3 facility

The exercise was performed with two different models of casualty triage. Triage Model A assumes a distribution of casualties to initial treatment facilities as follows: direct admission to Echelon 1 (33%); admission to Echelon 3 following resuscitation at Echelon 2 (33%); and admission to Echelon 3 following resuscitation and operation at Echelon 2 (33%). Triage Model B assumes that all WIA would be triaged to and resuscitated at the Echelon 3 facility. Since frozen red cell capability is only available at the Echelon 3 facility, this triage model would test the frozen red cell bank in the worst case scenario. Distribution of injuries by hemorrhage classification and triage route is outlined for Triage Model A and Triage Model B in Tables 3 and 4 respectively.

With a casualty rate of 6 WIA/1000 soldiers/day during a 5-day battle, 180 casualties would be incurred, with 135 WIA in shock. Red blood cell requirements would be expected to reach 98 units/day, with a 9-day total requirement of 490 units in Triage Model A (Table 5) and 130 units/day with a 9-day total

requirement of 650 units in the Triage Model B (Table 6). If the blood bank prepared the maximum number of units of frozen red cells per day with 4 processors, starting one day before the first casualties occurred and using a 24-hour post-wash storage period for the previously frozen red blood cells, the needs of the Echelon 3 facility could be met (Table 7).

The calculation of crystalloid requirements in these scenarios represents the volume required for resuscitation and maintenance fluids, but does not include that spilled or lost with incompletely infused intravenous bags, or that used during infusion of medications. Since each unit of previously frozen red cells utilizes 1.6 liters of crystalloid solution in the washing process, the supply of crystalloid solution required would depend on the number of frozen red blood cell units used. An on-site system would be used for preparation of the crystalloid solutions and the 0.9% sodium chloride and 0.2 gm% glucose solution used for post-thaw washing of the glycerol-frozen red blood cells.

In this scenario, the maximum requirement for crystalloid is on day 5 when blood utilization is highest. Approximately 486 liters of crystalloid solution would be required in Triage Model A and 642 liters in Triage Model B for preparation of the blood products and crystalloid solutions. One crystalloid processing system could produce 40 liters per hour and a maximum output of

960 liters per 24-hour period, amounts sufficient to meet the operating room requirements of Triage Models A and B.

Operating room requirements for an Echelon 3 facility during high-intensity combat under Triage Model A, with 180 wounded-in-action, are estimated to be approximately 130 major and minor operations (Table 8) over a 9-day period. As many as 26 major operations might be necessary in one day. As many as 171 operations might be performed at the Echelon 3 facility under Triage Model B.

This computer simulation permits testing for variables which might affect the efficiency of the frozen red cell blood bank system in meeting the needs of an Echelon 3 facility. If the processing efficiency dropped below 61% for Triage Model A and below 83% for Triage Model B, the blood bank would be unable to keep up with the demand. If the intensity of combat were to cause an increase in the average WIA/day for the duration of the combat, the frozen blood bank would be able to function at maximum efficiency only until the rate of WIA exceeded 10/day for Triage Model A, and 7.3/day for Triage Model B.

DISCUSSION

The successful care of combat casualties is related to the capabilities of the facility to which these casualties are triaged. These capabilities are affected by the size of the resuscitation area, the number and size of the operating rooms, and the physical capabilities for the care of patients postoperatively. In addition to the physical facilities, the composition of the personnel (qualifications and numbers), and the appropriateness of the logistic support are paramount in the success of the medical facility in meeting its mission.

Adequate care of war casualties requires sufficient quantities of resuscitative fluids and an efficient blood bank capable of meeting the demands of the treatment facility. The results of the simulation study described demonstrate that the processing of frozen red blood cells for the purpose of managing combat casualties would be labor and resource intensive. An Echelon 3 facility admitting 180 WIA in a five-day period must at peak times have the capacity to transfuse 130 units of red blood cells in a twenty-four-hour period.

Liquid preserved red blood cells have been successfully used in previous wars. The blood collection and preservation in the continental United States, transport at 4 C to an overseas site of conflict, and additional transport time to areas of use, required up to 15 days. Frozen red blood cells have several

advantages from a clinical and logistical perspective. Frozen red blood cells are safer than liquid preserved red blood cells, especially if the frozen red blood cells can be quarantined for 6 months and the donor re-examined for evidence of blood-borne pathogens before transfusion. Moreover, washed previously frozen red cells have some physiological advantages over liquid preserved red cells. Washed previously frozen red cells have 24 hour posttransfusion survival of 90%, whereas liquid preserved red blood cells have 24-hour posttransfusion survivals of 70%. Washed previously frozen red cells have near normal levels of 2,3 DPG and normal oxygen transport function, while liquid preserved red cells have decreased 2,3 DPG levels and impaired oxygen transport function.15

From a logistic perspective, the pre-positioning of frozen red cells at military medical facilities minimizes the need for a long supply line from the continental United States to the site of need. The logistic disadvantage is the need for -80 C freezers, special processing equipment, and trained personnel for processing, and the time necessary (one-hour) for post-thaw processing. Additional disadvantages are the need for large volumes of sterile crystalloid solution for the deglycerolization process. With the REFLUPS system, currently under evaluation, it would be possible to provide adequate volumes of crystalloid solution for deglycerolization of previously frozen red blood cells as well as for general resuscitative needs.

Under current military plans, Echelon 3 medical facilities will be supplied with 4 frozen blood processing units. With 3 to 4 technicians available at the facility to operate the processing systems for 22 of 24 hours/day, and assuming the systems perform without major breakdown, the blood bank should be able to process frozen red cells in numbers sufficient to meet the demands of an Echelon 3 facility in a mass casualty situation of five days duration.

An adequate supply of blood and crystalloid solution is indispensable in the care of casualties, but the capabilities of the medical treatment facility (facilities and personnel) are equally important. Estimates of operating room utilization provided by the simulation model described are that between 26 and 34 major operations will be performed in a 24-hour period. An Echelon 3 facility usually has six operating areas; this represents over five operations/area/day with the required nursing and technical staff and supplies to handle this operative caseload. Even if it is possible to meet the demand for red blood cells, the facility will not be able to fulfill its mission if the size and staff of the facility are not met.

The type of simulation model described is not limited to a military setting. The successful introduction of any new technology is dependent on a needs and benefits analysis.

Computer models based on accurate historic data can help predict the logistical problems of a new technology.

In conclusion, a simulation model can help pinpoint strengths and weaknesses of plans to care for mass casualties. This exercise demonstrates that the capacity to treat large numbers of patients in a short period of time is dependent upon both personnel and resources.

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TABLE 1

CLASSES OF ACUTE HEMORRHAGE AMERICAN COLLEGE OF SURGEONS ADVANCED TRAUMA LIFE SUPPORT MANUAL

	CLASS I			CLASS IV	
BLOOD LOSS (CC)	OD LOSS < 750		1500-1800	2000-2500	
BLOOD LOSS (%)	<15	20-25	30-35	40-50	

TABLE 2
ESTIMATED DAILY CRYSTALLOID AND BLOOD REQUIREMENTS

FOR

EACH PATIENT OVER ENTIRE HOSPITAL STAY STRATIFIED BY

CLASS OF HEMORRHAGE

CLASS OF HEMORRHAGE	SITE OF TRANSFUSION	DAY	CRYSTALLOID (liters)	BLOOD (units)
IV	RESUSCITATION AREA	1	6	2
IV	OPERATING ROOM	1	6	8
IV	ICU	1	5	2
IV	ICU	2	4	2 -
IV	ICU	3	4	2
īV	ICU	4	3	0
IV	ICU	5	3 •	0
			31	16
m	RESUSCITATION , AREA	1	4	0
Ш	OPERATING ROOM	1	4	2
m	ICU	1	4	2
ш	ICU	2	3	0
III	WARD	3	3	0
III	WARD	4	3	0
Ш	WARD	5	3	0
			24	4
П	RESUSCITATION AREA	1	3	0
II	OPERATING ROOM	1	i	2
II	WARD	2	2	0
11			ı	0
II	WARD	4	0	0
			8	2

MODEL A DISTRIBUTION OF CASUALTIES ADMITTED TO ECHELON 3 MEDICAL TREATMENT FACILITY FOLLOWING TRIAGE THROUGH ECHELON 1 AND ECHELON 2 MEDICAL TREATMENT FACILITIES

PARAMETERS = 5 DAY BATTLE 6 WIA/ 1000 SOLDIERS / DAY 6000 SOLDIERS AT RISK

TOTAL WIA=180

75% OF TOTAL WIA IN SHOCK= 135

DISTRIBUTION OF CASUALTIES IN SHOCK	% OF THOSE WIA IN SHOCK	WIA PER • DAY	5 DAY TOTAL
CLASS IV HEMORRHAGE	15%	4.05	20.25
DIRECT ECHELON 3 ADMIT	5%	1.35	6.75
AFTER ECHELON 1 OR 2, NO O.R.	5%	1.35	6.75
AFTER ECHELON 2 WITH O.R.	5%	1.35	6.75
CLASS III HEMORRHAGE	35%	9.45	47.25
DIRECT ECHELON 3 ADMIT	11.7%	3.15	15.75
AFTER ECHELON 1 OR 2, NO O.R.	11.7%	3.15	15.75
AFTER ECHELON 2 WITH O.R.	11.7%	3.15	15.75
CLASS II HEMORRHAGE	50%	13.5	67.5
DIRECT ECHELON 3 ADMIT	16.6%	4.5	22.5
AFTER ECHELON 1 OR 2, NO O.R.	16.7%	4.5	22.5
AFTER ECHELON 2 WITH O.R.	16.6%	4.5	22.5
TAL # OF ALL PATIENTS		27.0	135

MODEL B DISTRIBUTION OF CASUALTIES ADMITTED DIRECTLY TO ECHELON 3 HOSPITAL

PARAMETERS = 5 DAY BATTLE 6 WIA/ 1000 SOLDIERS / DAY 6000 SOLDIERS AT RISK

. TOTAL WIA=180

75% OF TOTAL WIA IN SHOCK= 135

DISTRIBUTION OF CASUALTIES IN SHOCK	% OF THOSE WIA IN SHOCK	WIA PER DAY	5 DAY TOTAL
CLASS IV HEMORRHAGE	15%	4.05	20.25
CLASS III HEMORRHAGE	35%	9.45	47.25
CLASS II HEMORRHAGE	50%	13.5	67.5
TOTAL # OF ALL PATIENTS		27.0	135

TRIAGE MODEL A

HOSPITAL REQUIREMENTS FOR BLOOD AND CRYSTALLOID BY BATTLE DAY 6 WIA / 1000 SOLDIERS / DAY

BATTLE DAY	BLOOD (units)	ON-SITE PREPARED CRYSTALLOID (liters)					
	(22.2)	RESUSCITATION	FROZEN RBC PROCESSING *	TOTAL			
1	82	143	123	265			
2	90	177	135	312			
3	98	258	147	405			
4	98	299	147	446			
5	98	339	147	486			
6	16	197	24	221			
7	8	125	12	138			
8	0	81	0	81			
9	0	40 0					
TOTALS	490	1660	735	· 2395			

^{*} Additional solution containing 50 ml 12% sodium chloride required for frozen red cell processing, currently not produced on-site.

TRIAGE MODEL B

HOSPITAL REQUIREMENTS FOR BLOOD AND CRYSTALLOID BY BATTLE DAY 6 WIA / 1000 SOLDIERS / DAY

BATTLE DAY	BLOOD (units)	ON-SITE PREPARED CRYSTALLOID (liters)					
2	(==)	RESUSCITATION	FROZEN RBC PROCESSING *	TOTAL			
1	113	236	170	406			
2	122	255	183	438			
3	130	366	195	561			
4	130	406	195	601			
5	130	447	· 195	642			
6	16	211	24	235			
7	8	126	12	138			
8	0	81	0	81			
9	0	41	0	41			
TOTALS	648	2168	974	3143			

^{*} Additional solution containing 50 ml 12% sodium chloride required for frozen red cell processing, currently not produced on-site.

TABLE 7

BLOOD BANK STORED BY BATTLE DAY BY TRIAGE MODEL

6 WIA/1000 SOLDIERS/DAY
4 PROCESSORS
1 UNIT/HOUR/PROCESSOR
24 HOUR SHELF-LIFE OF PROCESSED FROZEN BLOOD

BLOOD BANK BALANCE TRIAGE MODEL B	110 107 95 76 36 110 110
BLOOD TRANSFUSED TRIAGE MODEL B	1113 1122 1130 1130 16 0
BALANCE TRIAGE MODEL A	110 110 110 110 110 110 110
BLOOD TRANSFUSED TRIAGE MODEL A	0 8 8 8 8 8 0 0 0 0 0 0 0 0 0 0 0 0 0 0
BLOOD PROCESSED	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
BATTLE DAY	0122459786

TABLE 8

MAJOR OPERATIONS AT ECHELON 3 HOSPITAL BY BATTLE DAY BY TRIAGE MODEL

_											
	OPERATIONS- TRIAGE MODEL B	20	. 20	30	34	34	14	14	ۍ .	0	171
	OPERATIONS- TRIAGE MODEL A	13	13	23	26	26	13	13	3	0	130
	BATTLE DAY		. 2	3	4	5	9	7	80	6	TOTALS